UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/645,874	08/20/2003	Kenneth F. Buechler	36671-744.502	8658

80984 7590 10/02/2008

Inverness Medical Innovations / WSGR
Wilson Sonsini Goodrich & Rosati, P.C.
650 Page Mill Road
Palo Alto, CA 94304

EXAMINER	
LUM, LEON YUN BON	

ART UNIT	PAPER NUMBER
1641	

MAIL DATE	DELIVERY MODE
10/02/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/645,874	BUECHLER ET AL.	
	Examiner	Art Unit	
	Leon Y. Lum	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 August 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *29-33 and 43-46* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *29-33 and 43-46* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *See Continuation Sheet*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Continuation of Attachment(s) 3). Information Disclosure Statement(s) (PTO/SB/08), Paper No(s)/Mail Date :5/29/07, 7/25/07, 10/26/07, 8/8/08, 8/8/08.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on October 26, 2007 has been entered.

Information Disclosure Statement

The information disclosure statement filed May 29, 2007 fails to comply with the provisions of 37 CFR 1.97, 1.98 and MPEP § 609 because the A1 reference, US 6,117,744, seems to have been mislabeled. The name of the patentee is indicated as "Debold." However, the actual name is Ammo and the reference is directed to semiconductors. The patent number, therefore, seems to have been misnumbered. Accordingly, US 6,117,744 not been considered as to the merits. Applicant is advised that the date of any re-submission of any item of information contained in this information disclosure statement or the submission of any missing element(s) will be the date of submission for purposes of determining compliance with the requirements based on the time of filing the statement, including all certification requirements for statements under 37 CFR 1.97(e). See MPEP § 609.05(a).

The information disclosure statement filed May 29, 2007 also fails to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each cited foreign patent document; each non-patent literature publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. References A4 and A5, directed to a European search report and a definition from "Allwords," have not been provided. References A4 and A5, therefore, have not been considered.

The information disclosure statement filed July 25, 2007 fails to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each cited foreign patent document; each non-patent literature publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. Reference A8, directed to Griffin et al., has not been provided. The reference, therefore, has not been considered.

The information disclosure statement filed August 8, 2008 fails to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each cited foreign patent document; each non-patent literature publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. References 63, 68 and 71, directed to two European search reports and an International search report, are not provided. References 63, 68 and 71, therefore, have not been considered. Reference 55 also has not been considered, since it appears to be a repeat of reference 54.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 29, 32 and 43 are rejected under 35 U.S.C. 102(e) as being anticipated by Haffner *et al.* (US 2004/0167341) ("Haffner").

Haffner teaches a method for treating congestive heart failure by administering, to a patient, a compound that inhibits a dipeptidyl peptidase (DPP), including DPP-IV. *See* page 3, paragraphs 0027-0028 and 0030.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.

2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 30 and 44 are rejected under 35 U.S.C. 103(a) as being unpatentable over Haffner in view of De Meester *et al.* (Biochemical Pharmacology, vol. 54, pp. 173-179 (1997)) ("De Meester").

Haffner is disclosed above. Haffner, however, does not teach a dipeptide analogue comprising a phosphonate moiety.

De Meester teaches Prodipine (Pro-Pro-diphenyl-phosphonate) as a compound that blocks DPP-IV activity. *See* page 178, left column, 2nd-3rd full paragraphs. De Meester also teaches that Prodipine acts in both plasma and tissue, providing long-lasting results and functions without affecting any other enzyme or producing adverse effects upon the patient. *Id.*

Given the teachings of Haffner and De Meester, one of ordinary skill in the art at the time of the invention would have found it obvious to modify Haffner's method by administering Prodipine, a dipeptide analogue comprising a phosphonate moiety, as taught by De Meester. The skilled artisan would have been motivated to perform the modification based on De Meester's disclosure that Prodipine is long-lasting, functions in both plasma and tissue, and poses no adverse affects on a person taking the compound. Moreover, the skilled artisan would have had a reasonable expectation of success in combining the teachings of Haffner and De Meester, since Prodipine is one type of inhibitor that falls within the genus of inhibitors that act on DPP-IV, as taught by Haffner.

Claims 31 and 45 are rejected under 35 U.S.C. 103(a) as being unpatentable over Haffner in view of Bergmann *et al.* (US 6,756,483) ("Bergmann").

Haffner is disclosed above. Haffner, however, does not teach that the inhibitors of prolyl-specific DPP comprise an antibody or fragment thereof.

Bergmann teaches that inhibitors to DPP-IV include any suitable selective binder, antibody or similar receptor molecules. See column 3, lines 35-42.

The Federal Circuit and Board of Patent Appeals and Interferences have ruled that art-recognized equivalence presents a strong case for obviousness, where one material can be substituted for another. See MPEP 2144.06, citing *In re Ruff* and *Smith v. Hayashi*:

In order to rely on equivalence as a rationale supporting an obviousness rejection, the equivalency must be recognized in the prior art, and cannot be based on

applicant's disclosure or the mere fact that the components at issue are functional or mechanical equivalents. In re Ruff, 256 F.2d 590, 118 USPQ 340 (CCPA 1958) (The mere fact that components are claimed as members of a Markush group cannot be relied upon to establish the equivalency of these components. However, an applicant's expressed recognition of an art-recognized or obvious equivalent may be used to refute an argument that such equivalency does not exist.); Smith v. Hayashi, 209 USPQ 754 (Bd. of Pat. Inter. 1980) (The mere fact that phthalocyanine and selenium function as equivalent photoconductors in the claimed environment was not sufficient to establish that one would have been obvious over the other. However, there was evidence that both phthalocyanine and selenium were known photoconductors in the art of electrophotography. "This, in our view, presents strong evidence of obviousness in substituting one for the other in an electrophotographic environment as a photoconductor." 209 USPQ at 759.). An express suggestion to substitute one equivalent component or process for another is not necessary to render such substitution obvious. In re Fout, 675 F.2d 297, 213 USPQ 532 (CCPA 1982).

Here, Bergmann explicitly states that a selective binder, an antibody and similar receptor molecules are all appropriate inhibitors of DPP-IV. Consequently, one skilled in the art would recognize that, based on Bergmann's teachings, the aforementioned species of inhibitors are equivalent compounds for inhibiting DPP-IV. Applicants have not provided evidence to the contrary. Accordingly, it would have been obvious to one of ordinary skill in the art at the time of the invention to modify Haffner's method by substituting the pyrrolidines with antibodies specific for DPP-IV. Moreover, the skilled artisan would have had a reasonable expectation of success in combining Haffner's and Bergmann's teachings since antibodies, like pyrrolidines, can function *in vivo* to inhibit DPP-IV.

Claims 33 and 46 are rejected under 35 U.S.C. 103(a) as being unpatentable over Haffner in view of Mills *et al.* (Journal of the American College of Cardiology, vol. 34, no. 1, pp. 155-162 (1999)) ("Mills").

Haffner is described above. Haffner, however does not teach the step of administering natriuretic peptides to the subject.

Mills teaches the step of administering Nesiritide, a human B-type natriuretic peptide. *See* page 155, entire page. Mills also teaches that Nesiritide can maintain hemodynamic effects for patients with symptomatic decompensated heart failure. *Id.*

Given Haffner and Mills's teachings, one of ordinary skill in the art at the time of the invention would have found it obvious to modify Haffner's method by including Mills's Nesiritide. The skilled artisan would have been motivated to perform this modification based on Mills's disclosure that Nesitiride provides some benefit for patients with decompensated heart failure. Moreover, the skilled artisan would recognize that since DPP-IV inhibitors and Nesitiride act on congestive heart failure, the two compounds can be administered together. Accordingly, the skilled artisan would have had a reasonable expectation of success in combining the teachings of Haffner and Mills.

Response to Arguments

Applicant's arguments in the Supplemental Response, filed October 26, 2007, have been fully considered. These arguments are considered together with the arguments in the Response filed May 24, 2007, which accompanied an RCE. The arguments, however, are not persuasive to overcome the references as applied in the previous Office Action dated October 26, 2006. Accordingly, the previous rejections are maintained.

I. Claims 29, 32 and 43 Are Anticipated

A. *Haffner Properly Anticipates Claims 29, 32 and 43*

Applicants allege that Haffner does not teach the "selecting" step in claims 29, 32 and 43. *See* Supplemental Response, pages 4-6. It appears that Applicants' traversal of Haffner focuses on the notion that Haffner describes treatment and prophylaxis in the alternative and also provides a "wish list" of diseases that appears to be separate from the treatment/prophylaxis disclosure. *Id.* at page 5, 3rd paragraph. Applicants assert that this type of disclosure prevents the skilled artisan from recognizing that DPP is inhibited in a person who is selected "based upon a diagnosis of congestive heart failure," as claimed. *Id.* Applicants also supply a Rule 132 Declaration from Dr. Reilly providing the same arguments, in support of the traversal. Applicants' arguments, however, are not convincing for the following reasons.

Under § 102, a claim is anticipated "only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. v. Union Oil of California*, 814 F.2d 628, 631 (Fed. Cir. 1987); *see also* MPEP 2131. Here, Haffner explicitly teaches both prongs of the instant claims, i.e., the "selecting" and "administering" steps. *See* rejection *supra*. Indeed, Applicants do not deny that Haffner provides literal support for each prong. *See* Supplemental Response, page 5 (reciting the passage of Haffner that discloses a DPP-IV inhibitor and treating congestive heart failure). Accordingly, Haffner meets the test for anticipation, as set forth in the *Union Oil* case.

Given the requirements of a rejection under § 102, Applicants' foregoing arguments are not convincing. The mere fact that paragraphs 0027 and 0028, as written, do not overlap in their discussion of DPP inhibitors and treatment methods does not suggest that Haffner fails to teach DPP inhibitors for treating congestive heart disease. Indeed, paragraph 0030 indicates that the DPP inhibitors of paragraph 0027 are used to treat a patient with congestive heart failure, e.g. "the use of a ***compound of the present invention*** as herein described in the manufacture of a medicament for the ***treatment*** or prophylaxis of...***congestive heart failure***..." (emphasis added). Although not explicit in paragraph 0030, the stated compound can only be the DPP inhibitors of paragraph 0027, since they are the only compounds described in the disclosure. Indeed, as indicated by the title "Pyrrolidine as Dipeptidyl Peptidsase Inhibitors," and described throughout the disclosure, the focus of the reference is on DPP inhibitors. Consequently, the methods described therein, including the method of treating congestive heart failure, is linked to the DPP inhibitors.

Furthermore, the mere fact that (1) numerous diseases are listed and (2) both treatment and prophylaxis methods are disclosed does not attenuate the link between DPP inhibitors and treating, specifically, congestive heart failure. As written, Haffner teaches different combinations of treatments/prophylaxes for the different diseases listed. One of the combinations includes using DPP inhibitors to treat a patient with congestive heart failure. As set forth in the *Union Oil* case, anticipation is proper if each and every element is disclosed in one reference. Here, Haffner teaches each and every limitation, as claimed. Applicants' argument, therefore, does not properly traverse an

anticipation reference since the skilled artisan would recognize that Haffner teaches many different combinations, one of them including the specific treatment of congestive heart failure.

B. Haffner Is An Enabling Reference

Applicants opine that Haffner is not an enabling reference. *See* Supplemental Response, pages 6-10. Applicants support this assertion with an analysis using the Wands factors and the Rule 132 Declaration from Dr. Reilly. *Id.* Applicants' arguments, however, are not convincing for the following reasons.

i. The State of the Prior Art Indicates DPP-Inhibitor Relationship with Congestive Heart Failure

Dipeptidyl peptidase ("DPP"), as would have been known to the skilled artisan at the time of the invention, is a protease that cleaves proteins having proline in the penultimate position. *See* US 6,090,786 to Augustyns *et al.* ("Augustyns") at column 1, lines 33-39. The skilled artisan, therefore, would recognize that DPP would be able to cleave any protein fitting the profile of having proline in the penultimate position. Indeed, as evidenced by Augustyns, DPP-IV is capable of acting on different types of proteins, including neurotransmitter substance P, human growth hormone-releasing factor, erythropoietin, interleukin 2 and "many others." *Id.* at column 1, lines 49-59.

Brain natriuretic peptide ("BNP") is a natriuretic peptide known for treating cardiovascular disease, including congestive heart failure. Indeed, as cited in Applicants' response, a human recombinant BNP, Natrecor, has been approved by the FDA for treating patients with acutely decompensated congestive heart failure. *See*

Supplemental Response, page 8. Applicants also state that BNP, in combination with neutral endopeptidase inhibitors, "has been reported to produce a synergistic effect on cardiac output, reduced vascular resistance, and unloading of the heart." *Id.* at page 9. Moreover, BNP is a peptide with proline in the penultimate position. See US 5,786,163 to Hall at Sequence Listing spanning columns 5 and 6.

Given the skilled artisan's knowledge of DPP activity on proteins having proline in the penultimate position and the fact that BNP fits this profile, the skilled artisan would have recognized a nexus between DPP and BNP activity. As described above, Augustyns teaches that DPP can act on any protein with proline in the penultimate position; hence, the skilled artisan would have reasonably expected that DPP would also be capable of cleaving BNP. Moreover, since BNP is known to be associated with congestive heart failure, the skilled artisan would have also recognized the feasibility of a nexus between DPP inhibitors and congestive heart failure.

The prior art also provides evidence that DPP inhibitors are linked to cardiovascular function. For example, Papies et al. teaches that DPP-IV activity is increased in patients having arterial hypertension, suggesting a relationship between DPP-IV and cardiovascular disease. *See* Papies et al., European Heart Journal, vol. 8 (abstract suppl. 2), pg. 163, P591 (1987).

Together, the aforementioned references indicate that the state of the prior art recognizes a relationship between DPP inhibitors and congestive heart failure.

ii. The Relative Skill of Those in the Art

The skilled artisan is one having a high level of skill. The skilled artisan, moreover, would be able to recognize how to administer the DPP inhibitor compounds of Haffner to treat the listed diseases therein.

iii. The Predictability of the Art

As described above, the skilled artisan would recognize a clear relationship between DPP inhibitors and congestive heart failure. Although the Reilly declaration opines that the "vast majority" of the listed diseases in Haffner have not known direction relationship to DPP or DPP inhibitors (*see* Supplemental Response, page 9), the Augustyns and Papies references, along with Applicants' own statements in the Supplemental Response, indicate that the skilled artisan would have recognized a nexus between DPP inhibitor activity and BNP in relation to congestive heart failure. Since DPP would be capable of cleaving BNP and altering its function, a DPP inhibitor would be expected to prevent DPP from cleaving BNP, thereby allowing BNP to treat congestive heart failure. Accordingly, the level of predictability is far from having "no scientific basis to predict success," as alleged by Applicants. Indeed, the skilled artisan would have a relatively high level of success in applying the teachings of Haffner, based on the known functions and structures of DPP inhibitors and BNP.

B. Weighed Against the Foregoing Arguments, Applicants' Wands Factor Analysis Is Not Convincing

Applicants' arguments, asserting that Haffner does not provide an enabling disclosure, focuses on the allegation that the skilled artisan would not have recognized a direct relationship between DPP or DPP inhibitors with congestive heart failure. *See*

(i) quantity of experimentation necessary, (ii) amount of direction or guidance presented, (iii) presence or absence of working examples, (iv) nature of the invention, (v) state of the prior art, (vi) relative skill of those in the art, and (vii) predictability or unpredictability in the art arguments on pages 7-10.

Against the teachings of Augustyns, Papies and Applicants' own recognition of what was recognized in the art, however, Applicants' arguments are not convincing. The foregoing arguments present a direct rebuttal against the assertion that the skilled artisan would not have recognized a relationship between DPP or DPP inhibitors and congestive heart failure. Indeed, the skilled artisan would have recognized such a relationship.

Accordingly, Haffner is an enabling reference, and the previous rejections against claims 29, 32 and 43 are maintained.

II. Claims 30-31, 33 and 44-46 Are Obvious

Applicants traverse the rejection of claims 30-31, 33 and 44-46 by alleging that Haffner, in combination with De Meester, Bergmann or Mills, do not present a *prima facie* case of obviousness since the secondary references do not remedy the alleged deficiencies of Haffner. *See* Supplemental Response, pages 11-13. However, as described *supra*, Haffner is a proper reference. Since Applicants have not provided arguments against the merits of the cited secondary references, the traversal against the instant claims is not convincing. The prior rejections against claims 30-31, 33 and 44-46, therefore, are maintained.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leon Y. Lum whose telephone number is (571) 272-2872. The examiner can normally be reached on Monday to Friday (8:30 am to 5:00 pm).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long V. Le can be reached on (571) 272-0823. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Leon Y. Lum/
Examiner, Art Unit 1641

/Mark L. Shibuya, Ph.D./
Supervisory Patent Examiner, Art Unit 1641